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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
1623	10

DATE MAILED: 01/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	10/069,974	RAUTH ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37 and 39-44* is/are pending in the application.

4a) Of the above claim(s) *27-37 and 39-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

Drawings

Figures 1a and 1b are objected to as they are not of sufficient quality. Accordingly, new drawings which are clear and legible are required in reply to this Office action.

Election/Restrictions

Applicant's election of Group I in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

An action on the merits of group I, claims 1-26, is contained herein below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 15, and 24 all contain the phrase "**in the presence of** a salt and polyethylene glycol". It is unclear as to what is intended by a reaction which occurs in the presence of another compound. Does applicant intend the agents to be in the same container, or in the same room, etc.? Clarity is respectfully requested.

Claims 1-3, 16, and 24 are indefinite wherein the claims all have a gap in the text following "characterized in that", wherein the gap leaves uncertainty as to whether text is missing from the claim.

Claim 9 is indefinite wherein the claim is drawn to the method of claim 1 wherein the salt is used at a "final concentration" of 5 **mmol/1** to 4 mol/l". It is unclear as to what is intended by a "final concentration", as there is no indication of an initial concentration. Additionally, the "l" for liter of "5 mmol/1" appears to have been mistyped as a 1 (number one).

Claim 10 is indefinite wherein the claim in drawn to a method of claim 1 wherein "polyethylene glycol is used in a final concentration of 5% by weight of 40% by weight." It is unclear as to what is intended by a "final concentration", as there is no indication of an initial concentration. Moreover, it is unclear what is intended by the recitation "of 5% by weight of 40% by weight". It is unclear as to what the percentages are based upon and how they relate to one another in the claim language.

Claims 11 and 12 recite the limitation "the nucleic acid". There is insufficient antecedent basis for this limitation in the claim. Claims 11 and 12 depend from claim 1, wherein claim 1 is drawn to a method for binding nucleic acids (plural), and does not provide proper antecedent support for a subsequent claim which is intended to limit "the nucleic acid" (singular).

Claim 12 is indefinite wherein the claim is drawn to "the nucleic acid is amplification products". It is unclear how the nucleic acid (singular) can be amplification products (plural). Moreover, it is unclear by what is intended by "amplification products".

Claim 20 is drawn to the method of claim 15, wherein "the nucleic acid obtained is subjected to a mass spectrometric analysis". It is unclear how this limitation is intended to

patentably effect the method of isolating or purifying nucleic acids as previously set forth in the claim from which this depends (claim 15).

Claim 21 is confusing wherein the claim is drawn to a method of "determining the nucleotide sequence of a nucleic acid", as a sequence is normally generated for a plurality of nucleotides or nucleic acids (a strand of nucleic acids for example), not a single nucleic acid. Sequencing normally deals with the order of the nucleotides in the polynucleotide sample, and it is unclear how one would obtain the order of a single nucleic acid.

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 4-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628).

Claim 1 of the instant application is drawn to a method of binding nucleic acids to a solid phase comprising: contacting a solution containing nucleic acids with a solid phase which has hydrophobic and hydrophilic groups on the surface and a binder solution comprising a salt and polyethylene glycol, whereby the nucleic acids reversibly and sequence-unspecifically bind to

the surface of the solid phase. Claim 2 provides that the hydrophobic groups are alkyl or aryl groups. Claim 4 provides that the hydrophilic groups are hydroxyl groups. Claim 5 provides that the solid phase is solid particles, and claim 6 provides they are magnetic. Claim 7 provides that salt is an alkali, alkaline earth and/or ammonium halide. Claim 8 limits the molar mass of the polyethylene glycol to 1,000-20,000 g/mol. Claim 9 limits the salt concentration to 5 mmol/l to 4 mol/l. Claim 10 provides the concentration of the polyethylene glycol is 5-40% based on the weight. Claim 11 limits the nucleic acid to DNA, and claim 12 provides that the nucleic acid is an amplification product. Claim 13 provides that single- or double-stranded nucleic acids are selectively bound.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23). The magnetic microparticles are taught to be coated with a silane coat, such as n-dodecyltriethoxysilane (comprising an alkyl hydrophobic group) and a functional group such as a carboxyl group or thiol group (both hydrophilic groups) wherein carboxyl groups comprise a hydroxyl group bound to a carbonyl group (column 3, lines 10-55). Hawkins teaches that salts such as NaCl, LiCl, $BaCl_2$, KCl, $CaCl_2$, $MgCl_2$, and CeCl (column 5, lines 46-57) (various alkali and alkaline earth halides). The salt concentration is taught to be from about 0.5M to 5.0M, and the polyethylene glycol is taught to be from about 7-13% while having a molecular weight of from about 6,000-10,000 (column 5, lines 35-65). Hawkins additionally teaches that DNA and PCR amplification products can be used as the nucleic acids (column 6, lines 33-39, example 6).

Moreover, the polynucleotide is taught to be either single or double stranded (column 6, lines 60-62).

Claims 15-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628).

Claim 15 is drawn to a method of isolating or purifying nucleic acids comprising the steps of: contacting a solution containing nucleic acids with a solid phase which has hydrophobic and hydrophilic groups on the surface and a binder solution comprising a salt and polyethylene glycol, whereby the nucleic acids reversibly and sequence-unspecifically bind to the surface of the solid phase, separating the solid phase from the solution, and optionally detaching the nucleic acid from the solid phase. Claims 16 and 19 provide that the solid phase is magnetic and the solid phase is separated (from the nucleic acid) by magnetic means. Claim 17 provides that the solid phase is washed with a buffer solution which detaches impurities bound to the solid phase but not the nucleic acids. Claim 18 provides that the nucleic acids are detached using an elution solution.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23) as set forth supra. Moreover, Hawkins teaches that nucleic acid bound microparticles can be separated from the supernatant by applying a magnetic field, and once separated from the supernatant, the DNA can be removed from the magnetic microparticles by washing with an elution buffer, wherein the elution buffer comprising the nucleic acids can be separated from the

magnetic microparticles by applying a magnetic field (column 6, lines 3-28). Moreover, the magnetic microparticles with bound DNA can be washed with a buffer solution before separating the DNA so that impurities bound to the DNA molecule or microparticle are dissolved and the DNA remains attached to the microparticle (column 6, lines 30-59).

Claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628).

Claim 21 is drawn to a method of determining the nucleotide sequence of a nucleic acid comprising binding a nucleic acid to a solid phase by the method of claim 1 as set forth supra, and additionally by sequencing the nucleic acid by known methods. Claim 22 provides that the sequenced product is then purified.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23) as set forth supra. Additionally, Hawkins teaches that the nucleotide sequence bound to the magnetic microparticles can be determined by using conditions suitable for sequence determination which are known in the art (column 8, lines 41-52). Hawkins then teaches to purify the product by electrophoresis (example 5).

Claims 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628).

Claim 25 is drawn to a kit for practicing the method as set forth supra comprising, a binding buffer which contains a salt and polyethylene glycol, and a solid phase which has

hydrophobic and hydrophilic groups on its surface. Claim 26 adds an elution buffer to detach the nucleic acid from the surface and a washing buffer to separate the impurities to the kit of claim 25.

Hawkins teaches a kit for practicing the methods as set forth supra comprising the magnetic microparticles as set forth supra with a binding buffer. Moreover, Hawkins teaches there can be additionally an elution buffer to detach the nucleic acid from the solid phase and a wash buffer for removing the impurities (column 8, line 53 – column 9, line 15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determining the scope and contents of the prior art.
Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hawkins (US Patent 5,705,628) in view of Tang et al. (5,668,268).

Claims 1, 2, 4-13, 15-19, and 21-22 are drawn to he methods as set forth supra. Claim 3 further limits the method of claim 1 by stating that the alkyl groups of claim 2 are preferably C_8 or C_{18} alkyls, or mixtures thereof. Claim 14 provides that the nucleic acids are preferably in the range of from 5-1000 nucleotides. Claim 20 provides that the product of claim 15 is further subjected to mass spectrometric analysis. Claim 23 is drawn to a method of synthesizing nucleic acids comprising binding a nucleic acid to a solid phase as in claim 1, then extending the nucleic acid by known methods. Claim 24 is drawn to a method of detecting an analyte in a sample comprising attaching a nucleic acid to a solid phase as set forth supra, the contacting the solid phase with an analyte and determine if the analyte bound to the nucleic acids.

It is noted that these additional limitations are not seen to be critical and obvious to one of ordinary skill in the art. Applicant's method of claim 23 which comprises "extending the nucleic acid by at least one nucleotide by known methods", for example, shows that nothing is added to the claim which is not already known in the art. Additionally, the use of the C_8 or C_{18} alkyl groups is not seen to be critical, but merely optimizing an art recognized method. There are no data or examples in the disclosure which would afford the skilled artisan evidence that these limitations are anything more than a preferred embodiment of the prior arts known methods. Additionally, Hawkins is silent to the length of the nucleic acids, however, they do clearly state that nucleic acids can be separated based on size (column 7, lines 18-55) wherein Hawkins indeed contemplates the fact that various nucleic acids are eluted at varying polyethylene glycol concentrations. Moreover, the method of claim 24 is seen to be an obvious variant to the method of Hawkins, as analytes are known to be any chemical substance which is to be analyzed, and

one of skill in the are would recognize and understand methods of detecting an analyte using the method of Hawkins.

It is noted that applicants main focus is seen to be the use of both hydrophobic and hydrophilic functional groups attached to a magnetic microparticle, and subsequent attachment of nucleic acids while in a solution of polyethylene glycol and a salt. Hawkins renders this method obvious since a compound and its properties are inseparable. To use a compound in a manner to exploit it's properties is prima facia obvious. Moreover, the examiner would like to make of record Tang et al. (US Patent 5,668,268) which teaches methods of synthesizing and purifying oligonucleotides wherein a plurality of microparticles which have hydroxyl or amino groups are utilized which have had some of the hydrophilic hydroxyl or amino groups modified to hydrophobic groups by attaching a phenyl group to a portion of the hydrophilic hydroxyl or amino groups.

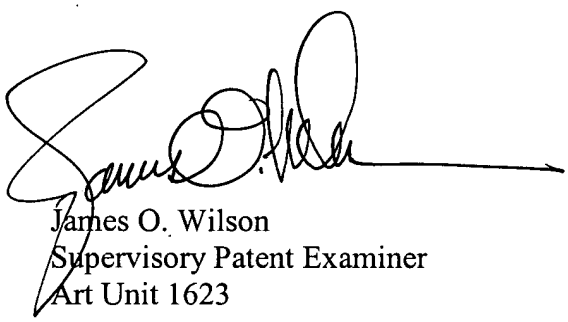
The claims of the instant application must contain new and patentable measures over the prior art to be patentable.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh
January 9, 2004